DOCKET NO.: ISIS-4288 Application No.: 09/438,989

Amendments to the Specification:

Please replace the paragraph on page 1, beginning at line 5, with the following replacement paragraph:

This patent application is a continuation-in-part of Application Serial Number 09/352,058, filed July 14, 1999 entitled "Oligonucleotides Having Site Specific Chiral Phosphorothioate Internucleoside Linkages", now U.S. Patent 6,440,943, which is a continuation-in-part of Application Serial Number 09/115,027 filed July 14, 1998 entitled "Phosphorothioate Oligonucleotides Having Modified Internucleotide Linkages", now U.S. Patent 6,242,589 the contents of which is incorporated herein by reference in their entirety.